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The influence of iodine deficiency during pregnancy on child neurodevelopment 0-24 months of age in East Java, Indonesia

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Abstract

Background: Development of the nervous system depends on an adequate intake of iodine. Infants and preschool-age children are vulnerable to iodine deficiency. Data is lacking on early neurodevelopmental of young children residing in iodine deficient area (IDA) and iodine-replete area (IRA). *Objectives and methods:* To investigate the effect of iodine deficiency during pregnancy on child development, by comparing the early development of children in an IDA, IRA with a non iodine-deficient area (NIDA) in Java, Indonesia. *Results*: Children from 0-24 months of age in IDA showed delay in fine motor, adaptation, personal-social, communication and gross motor development when compared to children in NIDA. Children in IRA fared better, but were also abnormal except in gross motor development. The somatic growth of these children were normal. Strabismus was the most common clinical finding seen in 25.7% of children in IDA, and 14.9% in IRA.
Conclusion: Iodine deficiency during pregnancy affect global neurodevelopment of young non-cretinous children.

INTRODUCTION

Development of the nervous system depends on adequate intake of iodine.[1] The consequences of iodine deficiency depends on the severity of the deficiency, but also the fetal age. A fetus's thyroid gland first begins to function in the 10-12th weeks, and the nerve cells begin to multiply between 10-18th weeks.[2] It is in this critical period that iodine deficiency may be detrimental to neurodevelopment. The mechanism of endemic cretinism is likely to be due to inadequate production of both maternal and fetal thyroid hormone as a result of iodine deficiency.[3]

Endemic cretinism is a severe form of brain damage due to iodine deficiency during prenatal life. Djokomoeljanto (1974)[4] in his study in Central Java found that the cretins were characterized by irreversible mental retardation, deaf-mutism, severe neuromotor deficits, goiters, growth retardation, and clinical hypothyroidism.

Research on the mental and motor disorders that accompany endemic goiter and endemic cretinism has been taking place chiefly in the developing countries.[5-12] There are to date no detailed data available on the neurodevelopment pattern of the non-cretinous young children residing in an iodine-deficient area (IDA) or iodine replete area (IRA), although there are limited data mostly in cross-sectional studies of children living in an IDA. Ramirez *et al* (1969)[13] used the Gesell's scale to evaluate neuromotor development of the young non-cretinous children. They found the mean developmental quotient of children 9-18 months of age in the iodinated community to be 92.7 as compared to 89.0 in the non-iodinated community. However, the difference was not statistically significant. Bleichrodt *et al* (1989)[9] from Spain used the Bailey scales of infant development (mental and motor development scale) and showed significant differences between the iodine-deficient and the control groups. The control group's average score was 103.7 as compared to the mean of 93.6 from the iodine-deficient group. Very high scores were not found in the iodine-deficient group, and almost 15% of the group had scores below 80.

The aim of this study was to investigate the influence of iodine deficiency during pregnancy on child development in East Java, Indonesia, by comparing the pattern of child development from 0-24 months of age in an IDA and an IRA, with the children from a non iodine-deficient area (NIDA) as control.

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METHODS

The IDA, IRA and NIDA were identified by assessment through various indicators as recommended by WHO, UNICEF, and ICCIDD (1994).[14] They were based on measurement of thyroid size using palpation and measurement of iodine concentration in urine of the school-age children.

The IDA and IRA identified were in the Ngantang sub-district, Malang regency, East Java. All of the pregnant women before midgestation in those areas were enrolled in this study from November 1995 until July 1996. The study subjects were all the infants born to these mothers. The NIDA identified was Brumbung village, Mranggen, Demak in Central Java. The characteristics of this village were matched in term of socio-economic and educational levels with the Ngantang sub-district. Since the infants in NIDA were to represent 'normal' neurodevelopment, they were free from the known risk factors which can affect neurodevelopment.

The indicators of the iodine status in these areas were: *IDA*: Visual Goiter Rate (VGR) =12.6%; Total Goiter Rate (TGR) = 37.8%; Urinary Excretory Iodine (UEI) in median (25^{th} - 75^{th} percentile) = 47 (27-84) µg/L; *IRA*: VGR = 0.6%; TGR = 4.7%; UEI in median (25^{th} - 75^{th} percentile) = 130 (102-156) µg/L; *NIDA*: VGR = 0.0%; TGR = 0.2%; UEI in median (25^{th} - 75^{th} percentile) = 190 (154-231) µg/L.

The children in IDA, IRA, and NIDA identified for study were regularly assessed for development, using the van Wiechen battery[15], at an interval of 2 months. In the same visit, general and neurological status of the children was examined by a team consisting of the main investigator (BH) and 3 nutritionists.

van Wiechen battery for assessment of child development

The van Wiechen battery is used in Dutch consultation offices for baby health screening. This is a developmental test, not an IQ test. It is not a definitive predictor of current or future adaptive, and intellectual ability. This battery alerts the professional to possible problems. The van Wiechen battery is also used for research. This battery consists of a kit of inexpensive materials, a score sheet and the reference manual. It is administered by observing the child when asked to perform various tasks appropriate for his age. In some items, the evaluation is based on parental observations. The test is administered in a standardized manner with exact test materials. This battery is made up of 75 tasks or items, for children from birth to four years. These items are arranged in three components: 1) Fine motor, adaptation, personal-social development; 2) Communication development; 3) Gross motor development.[15] Since there are no numeric parameters used in the van Wiechen battery, for quantitative analyses purposes, we developed new variables in numeric parameters. The van Wiechen battery was translated from Dutch to Indonesian with minor adaptations.

The anthropometric measurements

The infant's body weight, length, and head circumference were also measured. Height and head circumference were taken using the calibrated ribbon scale, and measured to the nearest 0.1 cm. The midwives and the nutritionists performed these anthropometric measurements.

Ethical considerations

Ethical considerations followed all guidelines of the CIOMS (1991)[16] for human research. The study protocol was approved by the Ministry of Health and the Ministry of Research and Technology of Indonesia, and the financing of this study was partially by these institutions.

Statistical analyses

The distribution of the variables has been checked by the One sample Kolmogorov Smirnov test. Data are reported as mean ± SD for normally distributed parameter, and as median and 25^{th} - 75^{th} percentile for non-normally distributed parameter. Differences between groups were examined by the T-test for normally distributed parameters, and by the Mann-Whitney U test for parameters which were not normally distributed. For nominal as well as proportional data, the Chi-square / Fisher exact tests were used. The software package of SPSS (Windows version 7.5, SPSS Inc. Chicago IL) was used for all statistical analyses and a p value < 0.05 was considered significant.

RESULTS

There were 295 children in the IDA, 95 in the IRA and 125 in the NIDA in this study. Nine children in the IDA and IRA were absent in one item of examination, and they were regarded as linearly developing. There were 2 children in the IDA who moved to another area beyond the sub-

district, they were regarded as normal.

The somatic growth of infants in the IDA, IRA and NIDA is as shown in Table 1. As shown, there were no significant differences in body weight, body length and head circumference among those 3 groups of infants from 0 till 24 months of age. Table 2 shows the clinical findings among children in the IDA and the IRA by 24 months of age.

As shown in Table 2, there were no cases of goiter, clinical hypothyroidism, and deaf-mutism. The prominent clinical abnormality in the IDA was strabismus which was significantly more frequent than children from IRA ($p<0.01$). The frequency of febrile convulsions and grand mal seizures was relatively low.

Child development from 0 to 24 months according to the van Wiechen battery

The fine motor, adaptation, and personal-social development according to the van Wiechen battery among the children from 0 till 24 months of age in IDA, IRA and NIDA is shown in Table 3. Table 4 shows the communication development, and Table 5 the gross motor development.

As shown in Table 3, the children in IDA were significantly delayed in fine motor, adaptation, and personal-social development when compared to children in NIDA in all ages between 0-24 months. When comparing development of children in IDA with IRA, there was significant delay in ages 2-4 months, 6-14 months, 16-18 months, and 20-24 months. When comparing development of children in IRA with NIDA, there was delay in children in IRA except at the ages of 0-2 months, 4-6 months, 8-10 months, 12-14 months. Thus, children in IDA were delayed in fine motor, adaptation, and personal-social development when compared to NIDA. Children in IRA fared better than those from IDA, but still showed some delay when compared with those from NIDA.

As shown in Table 4, the children in IDA showed significant delay in communication development when compared to children in NIDA and IRA in all ages between 0-24 months. When comparing the development of children in IRA with NIDA, there was significant delay in the children from IRA during assessment at 0-2 months, 10-12 months, 14-20 months, and 22-24 months. Thus, children in IDA were delayed in communication development when compared to children in NIDA and IRA. Children in IRA fared better than those from IDA, but still showed some delay when compared to those from NIDA especially by 14 months.

As shown in Table 5, the children in IDA showed significant delay in gross motor development when compared to children in NIDA and IRA in all ages between 0-24 months. When comparing the development of children in IRA with NIDA, there was no significant difference.

DISCUSSION

The children from the IDA and IRA were from Ngantang sub-district, Malang regency in East Java, and NIDA were from Demak in Central Java. The groups were matched in socio-economic and educational levels. As shown in Table 1, there were no significant differences in the weight, length, and head circumference of the three groups of children. Thus, iodine deficiency during pregnancy does not appear to affect the somatic growth of the infants from 0-24 months.

As for the clinical examinations, there was significant increase in number of children with strabismus, seen in 25.7% of children from IDA, and 14.9 % of children from IRA. The strabismus was mostly concomitant-convergent affecting both eyes. Strabismus is often observed during oculomotor development in early life, but it often gradually disappear in the course of infancy.[17] Oculomotor palsy is a clinical manifestation of endemic cretinism. It is also seen less frequently in brain damage children including sporadic congenital hypothyroidism.[18] The absence of goiter and clinical hypothyroidism suggests that thyroid hormone deficiency after birth was unlikely to be involved. This is supported by children in IDA having a normal body length. Delay in growth of body length is an important sign of postnatal hypothyroidism.[19] The low incidence of febrile convulsions (1.3%) and epilepsy (0.4%) in IDA suggests that seizures is not a common manifestation of brain damage from maternal iodine deficiency. This is similar to other findings.[3]

The language and fine motor/problem-solving developments can be viewed separately for the first 24 or 30 months of life. If both components are delayed, it may indicate the presence of mental retardation. If one of the two sectors is delayed, the infant is at high risk for communicative disorder or later learning disability. [20]

The visual motor-adaptive function is clinically a useful developmental component, which very early in infancy transitions into problem-solving skills. In this component, upper extremity

Table 1. Comparison of the somatic growth among infants in the iodine-deficient, iodine-replete, and non iodine-deficient area*.

	IDA	IRA	NIDA	p
Body weight (kg)				
At birth	3.0 ± 1.1	3.2 ± 0.9	3.1 ± 0.9	ns
6 months	6.1 ± 0.8	6.2 ± 0.7	6.2 ± 0.7	ns
12 months	8.6 ± 0.9	8.7 ± 0.9	8.7 ± 0.8	ns
18 months	10.0 ± 1.0	10.0 ± 1.3	10.1 ± 0.8	ns
24 months	11.0 ± 0.9	11.0 ± 1.0	11.1 ± 0.9	ns
Body length (cm)				
At birth	48.2 ± 2.0	49.5 ± 2.2	50.1 ± 1.4	ns
6 months	64.6 ± 3.0	64.6 ± 2.3	64.7 ± 2.3	ns
12 months	71.6 ± 3.1	71.7 ± 2.4	71.8 ± 2.4	ns
18 months	77.9 ± 2.9	78.0 ± 2.4	78.2 ± 2.4	ns
24 months	81.8 ± 2.8	81.9 ± 2.2	82.0 ± 2.1	ns
Head circumference (cm)				
At birth	35.3 ± 0.5	35.6 ± 0.6	35.7 ± 0.5	ns
6 months	42.1 ± 1.6	42.6 ± 1.0	42.4 ± 1.2	ns
12 months	45.1 ± 1.5	45.6 ± 1.1	45.5 ± 1.2	ns
18 months	46.3 ± 1.3	47.0 ± 1.0	46.9 ± 1.1	ns
24 months	46.9 ± 1.3	47.6 ± 1.0	47.5 ± 1.0	ns

All values are expressed as mean ± SD.
* Repeated measures ANOVA; *p*= level of significance; ns= not significant
IDA: Iodine-deficient area; IRA: Iodine-replete area; NIDA: Non iodine deficient area

Table 2. Clinical findings among children in the iodine-deficient (IDA) and the iodine-replete area (IRA) at 24 months of age

Clinical findings	IDA (n=225)		IRA (n=94)	
	Frequency	%	Frequency	%
Head circumference < - 2SD	11	4.9	2	2.1
Goiter	-	-	-	-
Clinical hypothyroidism	-	-	-	-
Strabismus*	58	25.7	14	14.9
Febrile convulsion	3	1.3	-	-
Grand mal seizure	1	0.4	-	-
Deaf-mutism	-	-	-	-
Congenital anomaly	1	0.4	-	-
Severe developmental delay	2	0.9	-	-

* Significant difference ($p<0.01$) / Chi-Square test.

Table 3. Summary of comparisons of fine motor, adaptation, and personal-social development among children (0-24 months) in the iodine-deficient, iodine-replete, and non iodine-deficient area.

Age (in months) & scores	IDA (n=225)		IRA (n=94)		NIDA (n=125)		Levels of significance*		
	No.	%	No.	%	No.	%	IDA vs NIDA	IDA vs IRA	IRA vs NIDA
0.0 – 2.0							<0.01	ns	ns
1	38	16.9	9	9.6	5	4.0			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	187	83.1	85	90.4	120	96.0			
2.1 – 4.0							<0.01	<0.05	<0.01
1	19	8.4	4	4.3	-	-			
2	23	10.2	4	4.3	6	4.8			
3	54	24.0	24	25.4	12	9.6			
4	129	57.4	62	66.0	107	85.6			
4.1 – 6.0							<0.01	ns	ns
1	26	11.6	6	6.4	5	4.0			
2	109	48.4	34	36.2	27	21.6			
3	-	-	-	-	-	-			
4	90	40.0	54	57.4	93	74.4			
6.1 – 8.0							<0.01	<0.01	<0.05
1	22	9.8	8	8.5	-	-			
2	52	23.1	12	12.8	18	14.4			
3	-	-	-	-	-	-			
4	151	67.1	74	78.7	107	85.6			
8.1 – 10.0							<0.01	<0.01	ns
1	22	9.8	4	4.3	-	-			
2	50	22.2	7	7.4	2	1.6			
3	59	26.2	5	5.3	17	13.6			
4	94	41.8	78	83.0	106	84.8			
10.1-12.0							<0.01	<0.01	<0.05
1	22	9.8	3	3.2	-	-			
2	111	49.3	20	21.3	15	12.0			
3	-	-	-	-	-	-			
4	92	40.9	71	75.5	110	88.0			
12.1 –14.0							<0.01	<0.01	ns
1	77	34.2	10	10.6	7	5.6			
2	63	28.0	42	44.7	40	32.0			
3	-	-	-	-	-	-			
4	85	37.8	42	44.7	78	62.4			
14.1–16.0							<0.01	ns	<0.01
1	34	15.1	8	8.5	4	3.2			
2	45	20.0	14	14.9	4	3.2			
3	-	-	-	-	-	-			
4	146	64.9	72	76.6	117	93.6			

16.1–18.0							<0.01	<0.01	<0.01
1	34	15.1	3	3.2	-	-			
2	40	17.8	16	17.0	3	2.4			
3	86	38.2	30	31.9	44	35.2			
4	65	28.9	45	47.9	78	62.4			
18.1–20.0							<0.01	ns	<0.01
1	43	19.1	14	14.9	7	5.6			
2	57	25.3	26	27.7	17	13.6			
3	-	-	-	-	-	-			
4	125	55.6	54	57.4	101	80.8			
20.1–22.0							<0.01	<0.05	<0.01
1	69	30.7	14	14.9	13	10.4			
2	62	27.6	29	30.9	19	15.2			
3	-	-	-	-	-	-			
4	94	41.8	51	54.2	93	74.4			
22.1-24.0							<0.01	<0.01	<0.01
1	47	20.9	8	8.5	6	4.8			
2	61	27.1	15	16.0	7	5.6			
3	-	-	-	-	-	-			
4	117	52.0	71	75.5	112	89.6			

IDA = Iodine-deficient area; IRA = Iodine-replete area; NIDA = Non iodine-deficient area
Scores: 1 = very poor; 2 = poor; 3 = fair; 4 = good developed.
*Chi-square / Fisher exact tests; ns = not significant
Items of observation: eye focusing, eyes and head following, hands opening, watching movement of own hands, plays with the hands mid front, grasps objects in supine, holds cube - takes another cube in other hand, plays with both feet, pick object with thumb and index finger, play with give and take, piles up two cubes, explore surrounding.

Table 4. Summary of comparisons in communication development, between children (0-24 months) in the iodine-deficient, iodine-replete, and non iodine-deficient area

Age (in months) & scores	**IDA (n=225)**		**IRA (n=94)**		**NIDA (n=125)**		**Levels of significance***		
	No.	%	No.	%	No.	%	IDA vs NIDA	IDA vs IRA	IRA vs NIDA
0.0 – 2.0							<0.01	<0.01	<0.01
1	40	17.8	6	6.4	1	0.8			
2	46	20.4	10	10.6	5	4.0			
3	-	-	-	-	-	-			
4	139	61.8	78	83.0	119	95.2			
2.1 – 4.0							<0.01	<0.01	ns
1	15	6.7	-	-	-	-			
2	36	16.0	-	-	-	-			
3	-	-	-	-	-	-			
4	174	77.3	94	100	125	100			

4.1 – 6.0							<0.01	<0.01	ns
1	19	8.4	-	-	-	-			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	206	91.6	94	100	125	100			
6.1 – 8.0							<0.01	<0.01	ns
1	43	19.1	1	1.1	3	2.4			
2	14	6.2	20	21.3	16	12.8			
3	-	-	-	-	-	-			
4	168	74.7	73	77.7	106	84.8			
8.1 – 10.0							<0.01	<0.01	ns
1	31	13.8	3	3.2	2	1.6			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	194	86.2	91	96.8	123	98.4			
10.1-12.0							<0.01	<0.01	<0.01
1	103	45.8	20	21.3	2	1.6			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	122	54.2	74	78.7	123	98.4			
12.1 –14.0							<0.01	<0.01	ns
1	2	0.9	1	1.1	-	-			
2	58	25.8	2	2.1	3	2.4			
3	37	16.4	23	24.5	15	12.0			
4	128	56.9	68	72.3	107	85.6			
14.1–16.0							<0.01	<0.01	<0.01
1	70	31.1	14	14.9	-	-			
2	60	26.7	20	21.3	43	34.4			
3	-	-	-	-	-	-			
4	95	42.2	60	63.8	82	65.6			
16.1–18.0							<0.01	<0.01	<0.01
1	63	28.0	13	13.8	-	-			
2	45	20.0	7	7.4	10	8.0			
3	50	22.2	20	21.3	28	22.4			
4	67	29.8	54	57.4	87	69.6			
18.1–20.0							<0.01	<0.01	<0.05
1	33	14.7	13	13.9	6	4.8			
2	72	32.0	2	2.1	1	0.8			
3	-	-	-	-	-	-			
4	120	53.3	79	84.0	118	94.4			

20.1–22.0							<0.01	<0.01	ns
1	47	20.9	2	2.1	2	1.6			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	178	79.1	92	97.9	123	98.4			
22.1-24.0							<0.01	<0.01	<0.01
1	94	41.8	20	21.3	10	8.0			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	131	58.2	74	78.7	115	92.0			

IDA = Iodine-deficient area; IRA = Iodine-replete area; NIDA = Non iodine-deficient area
Scores: 1 = very poor; 2 = poor; 3 = fair; 4 = good developed.
*Chi-square / Fisher exact tests; ns = not significant
Items of observation: Responds if spoken to, social smile, vocal social response, utters varied sound, reacts if called by name, says "dada" or "gaga", jabbers during play, responds to verbal request, waves "bye-bye", says 2 "sound words" with meaning, says 3 words, understand play instruction, makes sentences of two words.

Table 5. Summary of comparison of the gross motor development between children (0-24 months) in the iodine-deficient, iodine-replete, and non iodine-deficient area

Age (in months) & scores	**IDA (n=225)**		**IRA (n=94)**		**NIDA (n=125)**		Levels of significance*		
	No.	%	No.	%	No.	%	IDA vs NIDA	IDA vs IRA	IRA vs NIDA
0.0 – 2.0							<0.01	<0.01	ns
1	-	-	-	-	-	-			
2	102	45.3	2	2.1	5	4.0			
3	23	10.2	12	12.8	8	6.4			
4	100	44.4	80	85.1	112	89.6			
2.1 – 4.0							<0.01	<0.01	ns
1	-	-	-	-	-	-			
2	63	28	4	4.3	7	5.6			
3	23	10.2	8	8.5	-	-			
4	139	61.8	82	87.2	118	94.4			
4.1 – 6.0							<0.01	<0.01	ns
1	1	0.4	-	-	-	-			
2	22	9.8	1	1.1	-	-			
3	67	29.8	9	9.6	15	12.0			
4	135	60.0	84	89.4	110	88.0			
6.1 – 8.0							<0.01	<0.01	ns
1	-	-	-	-	-	-			
2	31	13.8	-	-	1	0.8			
3	33	14.6	-	-	-	-			
4	161	71.6	94	100	124	99.2			

8.1 – 10.0							<0.01	<0.01	ns
1	2	0.9	-	-	-	-			
2	9	4.0	-	-	-	-			
3	49	21.8	10	10.6	6	4.8			
4	165	73.3	84	89.4	119	95.2			
10.1-12.0							<0.01	<0.01	ns
1	-	-	-	-	-	-			
2	16	7.1	2	2.1	-	-			
3	42	18.7	9	9.6	12	9.6			
4	167	74.2	83	88.3	113	90.4			
12.1 –14.0							<0.01	<0.05	ns
1	42	18.7	6	6.4	7	5.6			
2	16	7.1	5	5.3	1	0.8			
3	19	8.4	6	6.4	4	3.2			
4	148	65.8	77	81.9	113	90.4			
14.1–16.0							<0.01	<0.05	ns
1	15	6.7	1	1.1	-	-			
2	33	14.7	8	8.5	8	6.4			
3	-	-	-	-	-	-			
4	177	78.7	85	90.4	117	93.6			
16.1–18.0							<0.01	<0.01	ns
1	36	16.0	6	6.4	1	0.8			
2	-	-	-	-	-	-			
3	-	-	-	-	-	-			
4	189	84.0	88	93.6	124	99.2			
18.1–20.0							<0.01	<0.01	ns
1	20	8.9	1	1.1	-	-			
2	74	32.9	27	28.7	30	24			
3	-	-	-	-	-	-			
4	131	58.2	66	70.2	95	76			
20.1–22.0							<0.01	<0.01	ns
1	47	20.9	9	9.6	-	-			
2	72	32.0	25	26.6	45	36.0			
3	-	-	-	-	-	-			
4	106	47.1	60	63.8	80	64.0			
22.1-24.0							<0.01	<0.01	ns
1	15	6.7	2	2.1	1	0.8			
2	30	13.3	2	2.1	-	-			
3	-	-	-	-	-	-			
4	180	80.0	90	95.8	124	99.2			

IDA = Iodine-deficient area; IRA = Iodine-replete area; NIDA = Non iodine-deficient area
Scores: 1 = very poor; 2 = poor; 3 = fair; 4 = good developed.
*Chi-square / Fisher exact tests; ns = not significant
Items of observation: move both arms to same extent, move legs to the same extent, remains hanging when lifted up under the armpits, reactions to pulled-to-sitting, lifts chin off couch, lifts head in prone to 45°, looks around with head lifted to 90°, legs flexed or kicking when swaying vertically, rolls himself from back to stomach and from stomach to back, can hold head firmly erect in sitting position, sits on buttock with stretched legs, sits alone steadily, crawls forward in prone-crawl position, pull himself to stand, crawls abdomen off ground, cruises at rail, walks alone, throws ball without falling, picks up object from squatting position, walks well freely.

performance is evaluated as an expression of higher cortical functioning. As shown in Tables 3, the children in IDA were significantly delayed in fine motor, adaptation, and personal-social development when compared to children in NIDA in all ages between 0-24 months. Children in IRA fared better than those from IDA, but still showed some delay when compared with those from NIDA. Our results are consistent with the findings in previous studies[6-12], that visual motor problem solving was impaired among the older children in the IDA.

Similar results were observed in communication development. The children in IDA were significantly delayed when compared to children in NIDA in all ages from 0-24 months. Children in IRA fared better than those from IDA, but still show some delay when compared to those from NIDA especially by 14 months.

In the absence of a communication disorder or significant hearing impairment, language development represents the best predictor of future intellectual performance. Language development can be divided into two phases. The first represents the pre-linguistic phase, in which the infant makes guttural noises that become pre-word utterances. This later transition into second phase or linguistic phase at 12 months, when the infant develops a single word vocabulary with comprehension.[20] Our study showed that the language development, both the pre-linguistic and linguistic phases was impaired in children in IDA. Delay in language development was also reported in previous studies among older children.[6,7,11]

Development of the fine motor and language functions is dependent on the cortical brain development. Njiokiktjien[21] mentioned that the cortical fields for the manual motor function and for speech are in close proximity and also undergo structural changes, particularly in a frontal direction and when left-right differences occurs. In infancy, the hand motor function goes through a development of increasing precision and refinement, in elementary perceptual or motor processes. These are basic for later development of praxis, one of the higher cortical functions.

Our results demonstrated that children in IDA has global delay in their development in fine motor, adaptation, personal-social, language, as well as gross motor function. This is similar to previous reports that a low global IQ and DQ were observed among the school-age children living in the IDA[5-9,11], and delay in motor milestones.[22-24] This global delay suggests that these children are at high risk for the (later) problem of mental retardation or mental deficiency.[20] Our finding also supports the view that the influence of iodine deficiency during pregnancy does not affect a specific part of the brain, but wide areas of the brain are involved, either subcortical or cortical areas of the cerebral hemispheres as well as the cerebellum. Results of experimental studies[1], brain imaging[25,26], and autopsy[27] also support this conclusion.

Children in IRA showed a normal gross motor development, but significant delays in the fine motor-adaptive and the language domains, though less severe than children in IDA. This suggests that the gross motor development is more responsive to iodine supplementation than the other domains. Endemic cretinism is a severe form of brain damage from iodine deficiency. Although there is delayed motor development[22,23], cretins are able to walk, while their language-speech, fine motor-social adaptive and problem solving skills remain poor.[7] Unlike fine motor and communication development, the earliest gross motor activity is a conglomerate of early-automatic reactions (the primitive reflexes) which become suppressed during the first 3 to 6 months of life, and are not continuous with later motor skill development. Rolling from supine into prone position and back as "an inherited co-ordination complex of human motility" during the earlier state of ontogenic locomotion, is presumably of spinal and lower brain-stem origin. The ability to lift the head in supine position reflects the differentiation of vestibular brain mechanism. Kneeling, defined as the first change of the development of standing up, is supported by integration of cerebellum, brain stem and basal ganglia. Standing up and walking reflects the differentiation and integration of brain mechanism needed for the development of motility in a vertical position, in which cerebellum, brain stem, basal ganglia, and cortico-spinal mechanisms are involved. The parts of the brain that are responsible for gross motor function are thus mostly sub-cortical areas and cerebellum.

As for the delay in fine motor adaptation, personal-social and language development in children from IRA, it suggests that when iodine deficiency is mild or iodine intake marginal, the children born in this area is still at risk of developmental delay. Careful evaluation of the iodine status in such areas is always needed. As mentioned by Hetzel (2000)[28], the most common manifestation of iodine deficiency at all age groups is goiter, but its most important impact is on neuropsychological development. The concept

of iodine deficiency should include impaired brain development, brain damage and goiter. Our findings emphasize the importance of iodine supplementation program, its monitoring and evaluation, to prevent impaired neurodevelopment and brain damage.

In conclusion,

1. Iodine deficiency during pregnancy has impact on fine motor, adaptation, personal-social, communication (speech-language) and gross motor development of the children from 0-24 months of age. The children are at high risk of subsequent mental retardation or mental deficiency.

2. Developments of fine motor, adaptation, personal-social and language functions, which mostly depend on the development of cortical brain areas, are more affected than gross motor function, suggesting that cortical areas are more susceptible to brain damage from iodine deficiency.

3. The gross motor function develops better than other domains, suggesting that gross motor development is more responsive to iodine supplementation. Gross motor function is supported by integration of non-cortical brain areas, such as basal ganglia, brain stem, and cerebellum.

4. In moderate to severe iodine-deficient areas, iodine deficiency in pregnancy does not affect the growth of the body weight, body length and head circumference of children from 0-2 years of age. Concomitant-convergent strabismus is the most common clinical abnormality in these children.

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